REMARKS

Applicants respectfully request entry of the above amendments to the claims and reconsideration of the application in light of the amendments to the claims and the arguments presented below.

The pending claims are set forth above. Claims 20-21 and 40-43 are currently pending. Claim 20 is currently amended to correct an inadvertent typographical error. Support for the amendment can be found in claim 40. The amendments to the pending claims are made without prejudice or disclaimer, do not constitute amendments to overcome any prior art rejections under U.S.C. §§ 102 or 103, and are fully supported by the specification as filed. No new matter has been added as a result of the above amendments. The rejections set forth in the Office Action have been overcome by amendment or are traversed by argument below.

Applicants thank the Examiner for withdrawing rejections under 35 U.S.C. § 112 for indefiniteness, and under 35 U.S.C. § 102(b) in view of Mechetner et al. or Junkun et al.

1. Sequence Listing and Statement

Applicants submit herewith a sequence listing entitled "02-1270-A_Seq_list" and an amendment incorporating it into the specification. The sequence listing does not go beyond the scope of the specification and adds no new matter.

2. Claim Rejections under 35 USC §112, first paragraph

A) Claims 20, 21 and 40-43 stand rejected under 35 USC §112, first paragraph for claiming new matter. The Action asserts that GenBank Accession Nos. recited in claims 20, 40, 42 and 43 are not supported by the specification as filed. Specifically, the Action contends that the specification only provides a list of names of genes having altered gene expression in drug-resistant compared to sensitive cells and does not contain the corresponding GenBank Accession Nos. Furthermore, the Action asserts that the specification as filed does not provide sufficient support for the relationship of the names of genes associated with the GenBank Accession Nos. recited in the amended claim. Applicants respectfully traverse.

Newly-added claim limitations can be supported in the specification through express, implicit or inherent disclosure. MPEP § 2163 I B. In cases of inherent disclosure, the extrinsic evidence must make it clear that the missing descriptive matter is necessarily present in the thing described and that it would be recognized by the person skilled in the art. MPEP § 2163.07(a). Applicants submit that GenBank is a public database containing information on peptides, polypeptides, and nucleic acids, and that a person of ordinary skill in the art would appreciate that known genes, including all of the genes recited in Applicants' pending claims, are known and were known to be associated with a GenBank Accession No.

at the time the application was filed. Further, the skilled worker would appreciate that the GenBank Accession No. for any particular gene can be easily found by performing a simple search on the NCBI website. One of no more than ordinary skill in the art would, therefore, understand that all the genes listed in the specification are associated with a GenBank Accession No., and would be able to locate the corresponding GenBank Accession No. for each gene. Thus, the GenBank Accession Nos. were inherently disclosed in the application as filed and do not constitute a new matter.

Further, the Action has previously raised the issue of whether the skilled worker could unambiguously identify the genes recited in the specification. Applicants' position is that the skilled worker would know the identities of these genes, and the GenBank Accession Nos. were added to the pending claims to remove any ambiguity with regard to the identity of these genes. Applicants respectfully submit that they are not required to submit a Sequence Listing for such well-known genes, but have submitted one herewith, along with a declaration attesting to the fact that the sequences in the Sequence Listing are the sequences of the corresponding genes having the GenBank Accession Nos. at the time this application was filed.

Finally, the art-recognized status of these genes is evidenced by the inclusion of oligonucleotide probes specific for each recited gene in a commercially-available chip microarray (Affymettrix U133A), as set forth in Example 2 of Applicants' specification.

Applicants' position, that one of ordinary skill in the art would have recognized the identities of genes recited in the application as filed and hence that these genes are inherently within the knowledge of the skilled worker, is supported by the Rule 132 declaration of Dr. William Ricketts submitted herewith. Dr. Ricketts opines that the skilled worker would have recognized the identities of the genes recited in the application as filed based on the existence of probes specific for these sequences comprising a commercially-available microarray (Affymetrix Array U133A) as recited in Example 2 of the specification (¶4), as evidenced by prior or contemporaneous scientific literature references identifying these genes by name (¶8), and further as evidenced by the GenBank entries identified by Accession No. (¶¶5-6), and finally by the sequences themselves (¶¶5-7). Dr. Ricketts testimony establishes the knowledge inherent in the ordinarily-skilled worker, and that the skilled worker would recognize that the invention as claimed herein was in Applicants' possession at the time the application was filed.

Applicants respectfully request the Examiner to reconsider and withdraw the asserted ground of rejection.

B) Claims 20, 21 and 40-43 stand rejected under 35 USC §112, first paragraph for failing to comply with the written description requirement. The Action asserts that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that

the inventor(s) at the time the application was filed had possession of the claimed invention. More specifically, the Action asserts that the claims recite GenBank Accession Nos. for which no structural identity is provided by nucleotide or amino acid sequence in the specification at the time of filing and that one skilled in the art cannot determine from the written disclosure of the specification alone whether the sequence as claimed is identical to the sequence contained in the database under the GenBank Accession No. at the time the application was filed. The Action further asserts that one skilled in the art cannot determine based on the Genbank Accession No. alone which entry for a sequence is being claimed if the sequence entry is modified or revised after the time of application filing or if a new sequence entry is added to the Accession No after the application's filing date.

The basis in the Action for finding Applicants' previous argument regarding public accessibility to be unpersuasive appears to be that although GenBank Accession Nos. are available on a public database, they could change in time and the Office could not determine that the sequence as claimed is identical to the sequence contained in the database under those Accession Nos.

Applicants respectfully traverse. Applicants respectfully submit that one of skill in the art need not disclose in detail what is conventional or well known in the art. *Hybritech Inc. v. Monoclonal Antibodies Inc.* 802 F2d 1367, 1384 (Fed. Cir. 1986), *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 1534 (Fed. Cir. 1987), MPEP § 2163 II A III. Knowledge that known genes are associated with corresponding GenBank Accession Nos. is common-place in the art. Additionally, all GenBank Accession Nos. recited in the claims were available on a public database (GenBank) *at the time of filing* of the application. Applicants, therefore, need not provide GenBank Accession Nos in the specification to prove that they were in possession of claimed invention. Similarly, Applicants need not disclose nucleotide or amino acid sequences corresponding to each Accession No. as one of skill in the art could have ascertained sequence for each Accession No. at the time of filing of the application by performing a simple search in GenBank database. Consequently, the sequences were also disclosed in the application at the time of filing of the application.

Applicants' also reiterate their contention that the art-recognized status of these genes is evidenced by the inclusion of oligonucleotide probes specific for each recited gene in a commercially-available chip microarray (Affymettrix U133A), as set forth in Example 2 of Applicants' specification.

Applicants' position, that one of ordinary skill in the art would have recognized the identities of genes recited in the application as filed and hence that these genes are inherently within the knowledge of the skilled worker, is supported by the Rule 132 declaration of Dr. William Ricketts submitted herewith. Dr. Ricketts opines that the skilled worker would have recognized the identities of the genes recited in the application as filed based on the existence of probes specific for these sequences comprising a commercially-available microarray (Affymetrix Array U133A) as recited in Example 2 of the

specification (¶4), as evidenced by prior or contemporaneous scientific literature references identifying these genes by name (¶8), and further as evidenced by the GenBank entries identified by Accession No. (¶¶5-6), and finally by the sequences themselves (¶¶5-7). Dr. Ricketts testimony establishes the knowledge inherent in the ordinarily-skilled worker, and that the skilled worker would recognize that the invention as claimed herein was in Applicants' possession at the time the application was filed.

The Action notes that the sequence for urokinase receptor (AY194849) was first available on the public database after the filing of the priority application. Applicants respectfully submit that the filing date of the current application, and not its priority date, is relevant in determining availability of Accession Nos. on the public database at the time of filing of the application.

Without conceding to the correctness of the Patent Office position and in an effort to expedite prosecution, Applicants submit herewith a Sequence Listing for these genes, along with a declaration attesting to the fact that the sequences in the Sequence Listing are the sequences of the corresponding genes having the GenBank Accession Nos. at the time this application was filed. Applicants note in this regard that they were under no obligation to disclose these sequences in the application as filed, in view of the knowledge of the skilled worker. *Capon v. Eshhar*, 418 F.3d 1349 (Fed. Cir. 2005)

Finally, Applicants thank the Examiner for pointing out that zinc finger protein (AP060181) does not exist with the provided Accession No. in any protein and nucleotide database. Applicants respectfully submit that the Accession No. recited for zinc finger protein in claim 20 was incorrect. Applicants have amended the claim to correct the inadvertent mistake.

In view of the foregoing, Applicants respectfully request the Examiner to reconsider and withdraw this ground of rejection.

C) Claims 20, 21 and 40-44 stand rejected under 35 USC §112, first paragraph for failing to comply with the enablement requirement. The Action asserts that the claims contain subject matter which was not described in the specification in such a way as to enable one of skill in the art to make or use the invention. Specifically, the Action asserts that one of skill in the art cannot extrapolate teachings of the specification to the scope of the claims. According to the Action, the specification teaches identifying differential gene expression between sensitive and resistant tumor cells, whereas, the claims are drawn to a method of identifying taxane resistant tumor by determining differential expression of genes between the tumor and normal tissue (or cells). The Action, therefore, asserts that the specification does not provide any teaching or objective evidence to show that taxane-resistant tumors or cells could be identified by comparing differential expression of genes between tumor cells and non-tumor cells, as recited in the pending claims.

The Action also asserts that neither the art of record nor the specification provide any teaching to identify taxane-resistant breast tumors or cells by comparing gene expression between tumor and non-tumor tissues or

cells when the tumor has not been exposed to any taxane drug, as recited in the pending claims. Consequently, the Action asserts, one of skill in the art would be forced into undue experimentation to practice the claimed invention. Applicants respectfully traverse.

Applicants respectfully submit that although their specification, in one aspect, teaches methods for identifying taxane-resistant cells by comparing gene expression in resistant and sensitive tumors (cells), the specification, in a second aspect, teaches method to identify taxane resistant cells by comparing gene expression in tumor and non-tumor cells when the cells have not been exposed to any drug.

As taught in the specification, resistance or sensitivity of cells to taxane can be an intrinsic property of cells, i.e. a property of cells prior to exposure to taxanes. (*See* Specification, page 16, lines 9-11). This intrinsic property is explored in Example 2 where the genes with differential expression in taxane resistant and sensitive cells are identified using the EDR assay (Table III). The EDR (Extreme Drug Resistance) assay refers to an assay performed on tumor cell samples without prior drug exposure to identify intrinsic drug resistance (*See* Specification, page 18, lines 1-5). To perform an EDR assay, tumor cells are exposed to a cytotoxic concentration of taxane for a period of 4 days, where the 4-day period is not sufficiently long to induce gene expression (*See* Specification pages 19-20). Genes identified by such EDR assay thus reflect intrinsic resistance of these cells.

In the instant case, the genes specifically recited in the pending claims (or in Table III) were identified using EDR assay on cells of either tumor or non-tumor origin followed by gene array analysis. Specifically, the cells used in the experiment were tumor cells, tumor-derived vascular endothelial cells (non-tumor cells) and cancer cell lines. The cells were first separated into resistant and sensitive cells by EDR assay as taught in Example 1 (*See* Specification page 27, lines 11-14) and, then, the gene expression profiles of resistant and sensitive cells were assessed using gene arrays. Since the cells were not treated with drugs for a sufficient time to select for drug resistance, the observed gene expression profiles reflected intrinsic gene expression in cells without exposure to drugs. Accordingly, the genes listed in Table III or in the pending claims reflect intrinsic drug resistance of these cells when the cells have not been exposed to a drug.

Additionally, the genes listed in Table III (or in the pending claims) were found to be differentially expressed in resistant cells of both tumor and non-tumor origin. Specifically, the genes were identified by overlapping differential gene expressions of resistant cancer cells, resistant endothelial (non-tumor) cells and resistant cancer cell lines. Thus, contrary to the assertion made in the Action, the specification teaches a method of identifying taxane resistant tumors and cells by determining differential expression of genes between the tumor and normal tissues (or cells).

In view of the foregoing discussion, Applicants respectfully request the Examiner to reconsider and withdraw this ground of rejection.

CONCLUSION

The Applicant respectfully contends that all conditions of patentability are met in the pending claims as amended or as originally presented. Allowance of the claims is thereby respectfully solicited.

If there are any questions or comments regarding this Response or application, the Examiner is encouraged to contact the undersigned representative as indicated below at 312-913-0001.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff LLP

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